IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: James Harrison Aylward	Art Unit	: to be assigned
Serial No.	: to be assigned	Examiner	: to be assigned
Filed	: June 21, 2001		
Title	: ANTI-CANCER COMPOUNDS		

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT FOR DIVISIONAL

Sir:

Applicant respectfully requests consideration of the remarks and entry of the amendment set forth herein. This preliminary amendment is filed with the transmittal papers for a divisional application under 35 U.S.C. §121 of United States Patent Application Serial No. (USSN) 09/486,199, filed February 22, 2000.

The following documents also are enclosed herewith:

- VERSION WITH MARKINGS TO SHOW CHANGES MADE

AMENDMENT

Please amend the above-captioned application as follows:

In The Specification:

Please amend the specification as follows.

Replace the title as filed with the following new title:

--METHODS OF STIMULATING THE IMMUNE SYSTEM--

On page 1, after the title on line 1, under the heading, insert:

--CROSS-REFERENCES TO RELATED APPLICATIONS

The present application is a divisional application of United States Patent Application Serial No. (USSN) 09/486,199, filed February 22, 2000, now pending, which was filed under 35 U.S.C. §371 based on PCT/AU98/00656, filed on August 19, 1998, which claims the benefit of priority to Australian Application No. PO-8640, filed August 19, 1997. These applications are explicitly incorporated herein by reference in their entirety and for all purposes.--

In The Claims:

Please cancel claims 1 to 32, without prejudice.

Please add the following new claims:

--33. A method of stimulating the immune system, the method comprising administering to the subject an effective amount of a compound,

wherein the compound is derived from an extract from the sap of a species of *Euphorbia*, wherein the compound

(a) is extractable from the *Euphorbia* sap in the presence of about 95% v/w ethanol,

(b) has cell inhibiting or retarding activity which is neither destroyed by acetone nor by heating at about 95°C for about 15 minutes, and

(c) is capable of inhibiting the growth of at least one cell line selected from the group consisting of MM96L, MM229, MM220, MM537, MM2058, HeLa, B16, LIM1215, A549, MCF7, MCC16 and Colo16.

34. The method of claim 33, wherein the *Euphorbia* species is selected from the group consisting of *Euphorbia peplus*, *Euphorbia drummondii* and *Euphorbia hirta*.

35. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a jatrophane, a jatrophane derivative and a pharmaceutically acceptable salt of a jatrophane or a jatrophane derivative.

36. The method of claim 35, wherein the compound comprises a composition comprising a jatrophane ring conformation.

37. The method of claim 36, wherein the jatrophane ring containing composition is present in two diastereomeric conformations.

38. The method of claim 36, wherein the jatrophane ring containing composition is present in one diastereomeric conformation.

39. The method of claim 38, wherein the diastereomeric conformation is a conformation II.

40. The method of claim 36, wherein the composition comprising a jatrophane ring conformation comprises a nicotinate moiety.

41. The method of claim 36, wherein the composition comprising a jatrophane ring conformation comprises a benzoate moiety.

42. The method of claim 36, wherein the composition comprising a jatrophane ring conformation comprises a iso-butyrate moiety.

43. The method of claim 33, wherein the jatrophane derivative comprises an ester derivative.

44. The method of claim 33, wherein the jatrophane derivative comprises an acetylated derivative.

45. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 1 position of a moiety selected from the group consisting of a -H and a -OAc.

46. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 2 position of a moiety selected from the group consisting of a -H, a -OAc and a CH_3.

47. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 3 position of a moiety selected from the group consisting of a -OH, a -OAc, a -OiBu ($O(CH_3)_2CHCO$), a -OCinn, a -OBz, a -$OBzOCH_2CO$, and a -$PhCH_2CH_2CO_2$.

48. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 4 position of an -H.

49. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 5 position of a moiety selected from the group consisting of a -OAc, a -OiBu ($O(CH_3)_2CHCO$), -OMeBu ($OCH_3CH_2CH(CH_3)CO$) and a -OAcAc.

50. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 6 position of a moiety comprising an exocyclic double bond.

51. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 7 position of an $-H_2$, a -OAc, a -OiBu ($O(CH_3)_2CHCO$), a -OmeBu ($OCH_3CH_2CH(CH_3)CO$), a -OPr, a -OCOiPr and a -OCOEt.

52. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 8 position of an $-H_2$, a -OH, a -OAc, a -OiBu ($O(CH_3)_2CHCO$), a -OmeBu ($OCH_3CH_2CH(CH_3)CO$), a -OBz and a -OAng.

53. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 9 position of an -OH, a -OAc ($-OCH_3CO$), a -OCinn (OPhCHCHCO) , a -ONic ($C_5H_4NCO_2$) and an = O.

54. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 10 position of a $-(CH_3)_2$.

55. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 11 and carbon 12 positions comprising a double bond between carbon 10 and carbon 11.

56. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 13 position of a $-(CH_3)$.

57. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 14 position of an -H, an -OH, a -OAc (OCH_3CO) and an = O.

58. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 15 position of an -OH and a -OAc (OCH_3CO).

59. The method of claim 35, wherein the composition comprises a 2,3,5,7,15-pentaacetoxy-9-nicotinoyloxy-14-oxojatropha-6(17),11E-diene (jatrophane 1) or a pharmaceutically acceptable salt.

60. The method of claim 35, wherein the composition comprises a 2,5,7,8,9,14-hexaacetoxy-3-benzoyloxy-15-hydroxy-jatropha-6(17),11*E*-diene (jatrophane 2) or a pharmaceutically acceptable salt.

61. The method of claim 35, wherein the compound comprises a 2,5,14-triacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxy-9-nicotinoyloxyjatropha-6(17), 11*E*-diene (jatrophane 3) or a pharmaceutically acceptable salt of these.

62. The method of claim 35, wherein the compound comprises a 2,5,9,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxyjatropha-6(17),11*E*-diene) (jatrophane 4) or a pharmaceutically acceptable salt of these.

63. The method of claim 35, wherein the compound comprises a 2,5,7,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-9-nicotinoyloxyjatropha-6(17),11E-diene (jatrophane 5) or a pharmaceutically acceptable salt of these.

64. The method of claim 35, wherein the compound comprises a 2,5,7,9,14-pentaacetoxy-3-benzoyloxy-8,15-dihydroxyjatropha-6(17),11E-diene (jatrophane 6) or a pharmaceutically acceptable salt of these.

65. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a pepluane, a pepluane derivative and a pharmaceutically acceptable salt of a pepluane or a pepluane derivative.

66. The method of claim 65, wherein the pepluane derivative comprises an ester derivative.

67. The method of claim 65, wherein the pepluane derivative comprises an acetylated derivative.

68. The method of claim 65, wherein the pepluane derivative comprises a substitution in a position in a pepluane skeleton selected from the group consisting of

an $-H_2$ or an -OAc ($-OCH_3CO$) at a carbon 1 position;

a $-CH_3$ and an -H at a carbon 2 position;

an -OBz at a carbon 3 position;

an -H at a carbon 4 position;

an -OAc ($-OCH_3CO$) at a carbon 5 position;

a $-CH_3$ or an $-CH_2OAc$ at a carbon 6 position;

an $-H_2$ at a carbon 7 position;

an -OAc ($-OCH_3CO$) or a double bond to C12 at a carbon 8 position;

an -OAc ($-OCH_3CO$) or a double bond to C18 at a carbon 9 position;

a $-CH_3$ and an -OAc ($-OCH_3CO$), a $-CH_3$, or a double bond to C11 at a carbon 10 position;

an $-H_2$ or a double bond to C10 at a carbon 11 position;

an -H or a double bond to C8 at a carbon 12 position;

a $-CH_3$ at a carbon 13 position;

an -OAc ($-OCH_3CO$) at a carbon 14 position;

an -OH at a carbon 15 position; and,

an -H or an $-H_2$ at a carbon 18 position.

69. The method of claim 65, wherein the pepluane comprises a composition selected from the group consisting of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane, a derivative of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane

and a pharmaceutically acceptable salt of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane.

70. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a paraliane, a paraliane derivative and a pharmaceutically acceptable salt of a paraliane or a paraliane derivative.

71. The method of claim 70, wherein the paraliane derivative comprises an ester derivative.

72. The method of claim 70, wherein the paraliane derivative comprises an acetylated derivative.

73. The method of claim 70, wherein the paraliane derivative comprises a substitution in a position in a paraliane skeleton selected from the group consisting of

an -H, an $-H_2$ or an -OAc ($-OCH_3CO$) at a carbon 1 position;

a $-CH_3$ and an -H or a $-CH_3$ and an -OAc ($-OCH_3CO$) at a carbon 2 position;

an -OBz at a carbon 3 position;

an -H at a carbon 4 position;

an -OAc ($-OCH_3CO$) at a carbon 5 position;

a $-CH_3$ or a $-CH_2OAc$ at a carbon 6 position;

an $-H_2$ at a carbon 7 position;

an -H or an -OAc ($-OCH_3CO$) at a carbon 8 position;

an = O at a carbon 9 position;

a $-(CH_3)_2$ at a carbon 10 position;

an $-H_2$ at a carbon 11 position;

an -H at a carbon 12 position;

a $-CH_3$ at a carbon 13 position;

an -OAc ($-OCH_3CO$) at a carbon 14 position; and,

an -OH at a carbon 15 position.

74. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a angeloyl-substituted ingenane, a angeloyl-substituted ingenane derivative and a pharmaceutically acceptable salt of a angeloyl-substituted ingenane or a angeloyl-substituted ingenane derivative.

75. The method of claim 74, wherein the angeloyl-substituted ingenane derivative comprises an ester derivative.

76. The method of claim 74, wherein the angeloyl-substituted ingenane derivative comprises an acetylated derivative.

77. The method of claim 74, wherein angeloyl-substituted ingenane is selected from the group consisting of a 20-O-acetyl-ingenol-3-angelate, an acetylated derivative of a 20-O-acetyl-ingenol-3-angelate and an ester derivative of a 20-O-acetyl-ingenol-3-angelate.

78. A method of stimulating the immune system, the method comprising administering to the subject an effective amount of at least two compounds,

wherein the two compounds are derived from an extract from the sap of a species of *Euphorbia*, wherein the compounds

(a) are extractable from the *Euphorbia* sap in the presence of about 95% v/w ethanol,

(b) have cell inhibiting or retarding activity which is neither destroyed by acetone nor by heating at about 95°C for about 15 minutes, and

(c) are capable of inhibiting the growth of at least one cell line selected from the group consisting of MM96L, MM229, MM220, MM537, MM2058, HeLa, B16, LIM1215, A549, MCF7, MCC16 and Colo16.

79. The method of claim 78, wherein the compounds are selected from the group consisting of a jatrophane, a jatrophane derivative, a pharmaceutically acceptable salt of a

jatrophane, a pepluane, a pepluane derivative, a pharmaceutically acceptable salt of a pepluane, a paraliane, a paraliane derivative, a pharmaceutically acceptable salt of a paraliane, an angeloyl-substituted ingenane, an angeloyl-substituted ingenane derivative and a pharmaceutically acceptable salt of an angeloyl-substituted ingenane.

80. The method of claim 78, wherein the compounds are selected from the group consisting of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane (pepluane), a derivative of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane, a 2,3,5,7,15-pentaacetoxy-9-nicotinoyloxy-14-oxojatropha-6(17),11E-diene (jatrophane 1), a derivative of a 2,3,5,7,15-pentaacetoxy-9-nicotinoyloxy-14-oxojatropha-6(17),11E-diene, a 2,5,7,8,9,14-hexaacetoxy-3-benzoyloxy-15-hydroxy-jatropha-6(17),11E-diene (jatrophane 2), a derivative of a 2,5,7,8,9,14-hexaacetoxy-3-benzoyloxy-15-hydroxy-jatropha-6(17),11E-diene, a 2,5,14-triacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxy-9-nicotinoyloxy-jatropha-6(17),11E-diene (jatrophane 3), a derivative of a 2,5,14-triacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxy-9-nicotinoyloxy-jatropha-6(17),11E-diene, a 2,5,9,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxyjatropha-6(17),11E-diene (jatrophane 4), a derivative of a 2,5,9,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxyjatropha-6(17),11E-diene, a 2,5,7,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-9-nicotinoyloxyjatropha-6(17),11E-diene (jatrophane 5), a derivative of a 2,5,7,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-9-nicotinoyloxyjatropha-6(17),11E-diene, a 2,5,7,9,14-pentaacetoxy-3-benzoyloxy-8,15-dihydroxyjatropha-6(17),11E-diene (jatrophane 6), a derivative of a 2,5,7,9,14-pentaacetoxy-3-benzoyloxy-8,15-dihydroxyjatropha-6(17),11E-diene, a 20-O-acetyl-ingenol-3-angelate, a derivative of a 20-O-acetyl-ingenol-3-angelate and pharmaceutically acceptable salt of one or any combination of these compounds.

81. The method of claim 78, wherein the compounds are provided in the form of a chemical fraction obtained from the sap of a species of *Euphorbia*.

82. The method of claim 33, wherein the compound further comprises a beta-alanine betaine or a hydroxy-dimethyl proline.

83. The method of claim 33, wherein the compound is capable of inhibiting or retarding the growth of MM96L cells.

84. The method of claim 33, wherein the compound is capable of inducing differentiation of MM96L cells.

85. The method of claim 33, wherein the compound is capable of inducing normal melanocytes to proliferate.

86. The method of claim 33, wherein the compound is capable of inducing T cells to proliferate.

87. The method of claim 33, wherein the compound is capable of inducing the expression of G-CSF.

88. The method of claim 33, wherein the compound is capable of inducing the expression of major histocompatibility complex (MHC) molecules.

89. The method of claim 33, wherein the compound is capable of recruiting a natural killer cell to a region of application of the compound.

90. The method of claim 33, wherein the compound is capable of a T cell to a region of application of the compound.

91. The method of claim 33, wherein the compound is provided in the form of a composition comprising a pharmaceutically- or cosmetically-acceptable carrier.

92. The method of claim 91, wherein the pharmaceutically- or cosmetically-acceptable carrier is selected from a β-alanine betaine hydrochloride and a t-4-hydroxy-N,N-dimethylproline.

93. A method of recruiting an immune cell to a region of application of a compound, the method comprising administering an effective amount of the compound to the region,

wherein the compound is derived from an extract from the sap of a species of *Euphorbia*, wherein the compound

(a) is extractable from the *Euphorbia* sap in the presence of about 95% v/w ethanol,

(b) has cell inhibiting or retarding activity which is neither destroyed by acetone nor by heating at about 95°C for about 15 minutes, and

(c) is capable of inhibiting the growth of at least one cell line selected from the group consisting of MM96L, MM229, MM220, MM537, MM2058, HeLa, B16, LIM1215, A549, MCF7, MCC16 and Colo16.

94. The method of claim 93, wherein a natural killer cell is recruited to the region of application of the compound.

95. The method of claim 93, wherein a T cell is recruited to the region of application of the compound.--

REMARKS

The Restriction Requirement and Election

The parent application was restricted to one of the following inventions under 35 U.S.C. §121:

I. Claims 1-10, drawn to a compound present in plants of the genus *Euphorbia* able to kill or inhibit the growth of cancer cells, or a composition containing a compound present in plants of the genus *Euphorbia* able to kill or inhibit the growth of cancer cells.

II. Claims 11-15, 20-21 and 25, drawn to a method of treatment of a cancer, comprising the step of administering an anti-cancer effective amount of a compound present in plants of the genus *Euphorbia* or a composition comprising a compound present in plants of the genus *Euphorbia*.

III. Claims 16-17, 20-21 and 25, drawn to a method of stimulating proliferation of non-neoplastic cells.

IV. Claims 18, 20-21 and 25, drawn to a method of alleviating disease conditions by stimulating cells of the immune system.

V. Claims 19-21 and 25, drawn to a method of inducing neoplastic cells to differentiate.

VI. Claims 22 and 24-25, drawn to a method of preventing or alleviating damage to skin caused by ultraviolet irradiation, ionizing radiation, microwave radiation or exposure to ozone.

In the parent, in response to the Restriction Requirement, Group II was elected

In the instant divisional application, after entry of the instant amendment, pending claims will be drawn to methods of stimulating cells of the immune system, Group IV.

Claims canceled and added in the instant amendment

Claims 1 to 32 are canceled, without prejudice, and new claims 33 to 95 are added. Thus, after entry of the instant amendment, claims 33 to 95 will be pending.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for new claims directed to methods of inducing the immune system wherein the compound is provided in the form of a ethanol extract obtained from the sap of a species of *Euphorbia* can be found, *inter alia*, in Example 12, on pages 52 to 53. Support

for new claims directed to methods wherein the compound is capable of inhibiting the growth of various cell lines, can be found, *inter alia*, on page 12, lines 20 to 26. Support for new claims directed to methods wherein the compound is provided in the form of an ethanol extract obtained from the sap of a species of *Euphorbia peplus*, *Euphorbia drummondii* or *Euphorbia hirta* can be found, *inter alia*, on page 12, lines 5 to 30. Support for new claims directed to methods wherein the compound can be a jatrophane, a jatrophane derivative or a pharmaceutically acceptable salt thereof, or a composition comprising a jatrophane ring conformation, including a composition is present in two diastereomeric conformations, can be found, *inter alia*, on Table 2, page 14 to 15; on page 42, line 27 to page 43, line 26; on page 45, line 15 to page 49, line 6. Support for new claims directed to methods wherein the compound can be a pepluane, a pepluane derivative and a pharmaceutically acceptable salt thereof, can be found, *inter alia*, on Table 2, page 14 to 15; on page 46, Table 15; page 47, lines 11 to 15. Support for new claims directed to methods wherein the compound can be a paraliane, a paraliane derivative and a pharmaceutically acceptable salt thereof can be found, *inter alia*, on Table 2, page 14 to 15; on page 13, lines 3 to 11. Support for new claims directed to methods wherein the compound can be an angeloyl-substituted ingenane, or a derivative of the angeloyl-substituted ingenane, or a pharmaceutically acceptable salt thereof, can be found, *inter alia*, on page 12, lines 5 to 35; Example 9, pages 43 to 45, e.g., page 45, lines 2 to 10; Example 10, pages 49 to 51, e.g., lines 23 to 25, page 49; Example 12, pages 52 to 53, e.g., lines 19 to 37, page 52. Support for new claims directed to methods of stimulating the immune system can be found, *inter alia*, on page 17, lines 13 to 21; page 56, lines 24 to 28; page 63, lines 1 to 14. Support for new claims directed to methods of recruiting natural killer and/or T cells to a region of application, can be found, *inter alia*, on page 63, lines 13 to 18. Support for new claims directed to methods wherein the compound is capable of inducing the expression of G-CSF and/ or major histocompatibility complex (MHC) molecules can be found, *inter alia*, on page 56, lines 5 to 8 and 24 to 28; and Table 19. Support for new claims directed to methods wherein the compound further comprises a beta-alanine betaine or a hydroxy-dimethyl proline, can be found, *inter alia*, page 16, lines 22 to 24.

CONCLUSION

In view of the foregoing amendment and remarks, Applicant believes all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicant believes that no fee is required for submission of this Response. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 06-1050. Please credit any overpayment to the above-noted Deposit Account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858 678 5070.

Respectfully submitted,

Date: June 21, 2007

Gregory P. Einhorn
Reg. No. 38,440

Fish & Richardson P.C.
4350 La Jolla Village Drive, Suite 500
San Diego, CA 92122
Telephone: (858) 678-5070
Facsimile: (858) 678-5099

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant : James Harrison Aylward
Serial No. : to be assigned
Filed : June 21, 2001
Title : ANTI-CANCER COMPOUNDS

Art Unit : to be assigned
Examiner : to be assigned

In The Specification:

On page 1, after the title on line 1, under the heading, the following paragraph has been inserted:

--CROSS-REFERENCES TO RELATED APPLICATIONS

The present application is a divisional application of United States Patent Application Serial No. (USSN) 09/486,199, filed February 22, 2000, now pending, which was filed under 35 U.S.C. §371 based on PCT/AU98/00656, filed on August 19, 1998, which claims the benefit of priority to Australian Application No. PO-8640, filed August 19, 1997. These applications are explicitly incorporated herein by reference in their entirety and for all purposes.--

In The Claims:

The following new claims have been added:

--33. A method of stimulating the immune system, the method comprising administering to the subject an effective amount of a compound,

wherein the compound is derived from an extract from the sap of a species of *Euphorbia*, wherein the compound

(a) is extractable from the *Euphorbia* sap in the presence of about 95% v/w ethanol,

(b) has cell inhibiting or retarding activity which is neither destroyed by acetone nor by heating at about 95°C for about 15 minutes, and

(c) is capable of inhibiting the growth of at least one cell line selected from the group consisting of MM96L, MM229, MM220, MM537, MM2058, HeLa, B16, LIM1215, A549, MCF7, MCC16 and Colo16.

34. The method of claim 33, wherein the *Euphorbia* species is selected from the group consisting of *Euphorbia peplus*, *Euphorbia drummondii* and *Euphorbia hirta*.

35. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a jatrophane, a jatrophane derivative and a pharmaceutically acceptable salt of a jatrophane or a jatrophane derivative.

36. The method of claim 35, wherein the compound comprises a composition comprising a jatrophane ring conformation.

37. The method of claim 36, wherein the jatrophane ring containing composition is present in two diastereomeric conformations.

38. The method of claim 36, wherein the jatrophane ring containing composition is present in one diastereomeric conformation.

39. The method of claim 38, wherein the diastereomeric conformation is a conformation II.

40. The method of claim 36, wherein the composition comprising a jatrophane ring conformation comprises a nicotinate moiety.

41. The method of claim 36, wherein the composition comprising a jatrophane ring conformation comprises a benzoate moiety.

42. The method of claim 36, wherein the composition comprising a jatrophane ring conformation comprises a iso-butyrate moiety.

43. The method of claim 33, wherein the jatrophane derivative comprises an ester derivative.

44. The method of claim 33, wherein the jatrophane derivative comprises an acetylated derivative.

45. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 1 position of a moiety selected from the group consisting of a -H and a -OAc.

46. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 2 position of a moiety selected from the group consisting of a -H, a -OAc and a CH_3.

47. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 3 position of a moiety selected from the group consisting of a -OH, a -OAc, a -OiBu ($O(CH_3)_2CHCO$), a -OCinn, a -OBz, a -$OBzOCH_2CO$, and a -$PhCH_2CH_2CO_2$.

48. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 4 position of an -H.

49. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 5 position of a moiety selected from the group consisting of a -OAc, a -OiBu ($O(CH_3)_2CHCO$), -OMeBu ($OCH_3CH_2CH(CH_3)CO$) and a -OAcAc.

50. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 6 position of a moiety comprising an exocyclic double bond.

51. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 7 position of an $-H_2$, a -OAc, a -OiBu ($O(CH_3)_2CHCO$), a -OmeBu ($OCH_3CH_2CH(CH_3)CO$), a -OPr, a -OCOiPr and a -OCOEt.

52. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 8 position of an $-H_2$, a -OH, a -OAc, a -OiBu ($O(CH_3)_2CHCO$), a -OmeBu ($OCH_3CH_2CH(CH_3)CO$), a -OBz and a -OAng.

53. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 9 position of an -OH, a -OAc ($-OCH_3CO$), a -OCinn (OPhCHCHCO) , a -ONic ($C_5H_4NCO_2$) and an = O.

54. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 10 position of a $-(CH_3)_2$.

55. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 11 and carbon 12 positions comprising a double bond between carbon 10 and carbon 11.

56. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 13 position of a $-(CH_3)$.

57. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 14 position of an -H, an -OH, a -OAc (OCH_3CO) and an = O.

58. The method of claim 36, wherein the jatrophane derivative comprises a substitution in the jatrophane ring carbon 15 position of an -OH and a -OAc (OCH_3CO).

59. The method of claim 35, wherein the composition comprises a 2,3,5,7,15-pentaacetoxy-9-nicotinoyloxy-14-oxojatropha-6(17),11E-diene (jatrophane 1) or a pharmaceutically acceptable salt.

60. The method of claim 35, wherein the composition comprises a 2,5,7,8,9,14-hexaacetoxy-3-benzoyloxy-15-hydroxy-jatropha-6(17),11*E*-diene (jatrophane 2) or a pharmaceutically acceptable salt.

61. The method of claim 35, wherein the compound comprises a 2,5,14-triacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxy-9-nicotinoyloxyjatropha-6(17), 11*E*-diene (jatrophane 3) or a pharmaceutically acceptable salt of these.

62. The method of claim 35, wherein the compound comprises a 2,5,9,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxyjatropha-6(17),11*E*-diene) (jatrophane 4) or a pharmaceutically acceptable salt of these.

63. The method of claim 35, wherein the compound comprises a 2,5,7,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-9-nicotinoyloxyjatropha-6(17),11E-diene (jatrophane 5) or a pharmaceutically acceptable salt of these.

64. The method of claim 35, wherein the compound comprises a 2,5,7,9,14-pentaacetoxy-3-benzoyloxy-8,15-dihydroxyjatropha-6(17),11E-diene (jatrophane 6) or a pharmaceutically acceptable salt of these.

65. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a pepluane, a pepluane derivative and a pharmaceutically acceptable salt of a pepluane or a pepluane derivative.

66. The method of claim 65, wherein the pepluane derivative comprises an ester derivative.

67. The method of claim 65, wherein the pepluane derivative comprises an acetylated derivative.

68. The method of claim 65, wherein the pepluane derivative comprises a substitution in a position in a pepluane skeleton selected from the group consisting of

an $-H_2$ or an -OAc ($-OCH_3CO$) at a carbon 1 position;

a $-CH_3$ and an -H at a carbon 2 position;

an -OBz at a carbon 3 position;

an -H at a carbon 4 position;

an -OAc ($-OCH_3CO$) at a carbon 5 position;

a $-CH_3$ or an $-CH_2OAc$ at a carbon 6 position;

an $-H_2$ at a carbon 7 position;

an -OAc ($-OCH_3CO$) or a double bond to C12 at a carbon 8 position;

an -OAc ($-OCH_3CO$) or a double bond to C18 at a carbon 9 position;

a $-CH_3$ and an -OAc ($-OCH_3CO$), a $-CH_3$, or a double bond to C11 at a carbon 10 position;

an $-H_2$ or a double bond to C10 at a carbon 11 position;

an -H or a double bond to C8 at a carbon 12 position;

a $-CH_3$ at a carbon 13 position;

an -OAc ($-OCH_3CO$) at a carbon 14 position;

an -OH at a carbon 15 position; and,

an -H or an $-H_2$ at a carbon 18 position.

69. The method of claim 65, wherein the pepluane comprises a composition selected from the group consisting of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane, a derivative of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane and a pharmaceutically acceptable salt of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane.

70. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a paraliane, a paraliane derivative and a pharmaceutically acceptable salt of a paraliane or a paraliane derivative.

71. The method of claim 70, wherein the paraliane derivative comprises an ester derivative.

72. The method of claim 70, wherein the paraliane derivative comprises an acetylated derivative.

73. The method of claim 70, wherein the paraliane derivative comprises a substitution in a position in a paraliane skeleton selected from the group consisting of

an -H, an $-H_2$ or an -OAc ($-OCH_3CO$) at a carbon 1 position;

a $-CH_3$ and an -H or a $-CH_3$ and an -OAc ($-OCH_3CO$) at a carbon 2 position;

an -OBz at a carbon 3 position;

an -H at a carbon 4 position;

an -OAc ($-OCH_3CO$) at a carbon 5 position;

a $-CH_3$ or a $-CH_2OAc$ at a carbon 6 position;

an $-H_2$ at a carbon 7 position;

an -H or an -OAc ($-OCH_3CO$) at a carbon 8 position;

an = O at a carbon 9 position;

a -$(CH_3)_2$ at a carbon 10 position;

an -H_2 at a carbon 11 position;

an -H at a carbon 12 position;

a -CH_3 at a carbon 13 position;

an -OAc (-OCH_3CO) at a carbon 14 position; and,

an -OH at a carbon 15 position.

74. The method of claim 33, wherein the compound comprises a composition selected from the group consisting of a angeloyl-substituted ingenane, a angeloyl-substituted ingenane derivative and a pharmaceutically acceptable salt of a angeloyl-substituted ingenane or a angeloyl-substituted ingenane derivative.

75. The method of claim 74, wherein the angeloyl-substituted ingenane derivative comprises an ester derivative.

76. The method of claim 74, wherein the angeloyl-substituted ingenane derivative comprises an acetylated derivative.

77. The method of claim 74, wherein angeloyl-substituted ingenane is selected from the group consisting of a 20-O-acetyl-ingenol-3-angelate, an acetylated derivative of a 20-O-acetyl-ingenol-3-angelate and an ester derivative of a 20-O-acetyl-ingenol-3-angelate.

78. A method of stimulating the immune system, the method comprising administering to the subject an effective amount of at least two compounds,

wherein the two compounds are derived from an extract from the sap of a species of *Euphorbia*, wherein the compounds

(a) are extractable from the *Euphorbia* sap in the presence of about 95% v/w ethanol,

(b) have cell inhibiting or retarding activity which is neither destroyed by acetone nor by heating at about 95°C for about 15 minutes, and

(c) are capable of inhibiting the growth of at least one cell line selected from the group consisting of MM96L, MM229, MM220, MM537, MM2058, HeLa, B16, LIM1215, A549, MCF7, MCC16 and Colo16.

79. The method of claim 78, wherein the compounds are selected from the group consisting of a jatrophane, a jatrophane derivative, a pharmaceutically acceptable salt of a jatrophane, a pepluane, a pepluane derivative, a pharmaceutically acceptable salt of a pepluane, a paraliane, a paraliane derivative, a pharmaceutically acceptable salt of a paraliane, an angeloyl-substituted ingenane, an angeloyl-substituted ingenane derivative and a pharmaceutically acceptable salt of an angeloyl-substituted ingenane.

80. The method of claim 78, wherein the compounds are selected from the group consisting of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane (pepluane), a derivative of a 5,8,9,10,14-pentaacetoxy-3-benzoyloxy-15-hydroxypepluane, a 2,3,5,7,15-pentaacetoxy-9-nicotinoyloxy-14-oxojatropha-6(17),11E-diene (jatrophane 1), a derivative of a 2,3,5,7,15-pentaacetoxy-9-nicotinoyloxy-14-oxojatropha-6(17),11E-diene, a 2,5,7,8,9,14-hexaacetoxy-3-benzoyloxy-15-hydroxy-jatropha-6(17),11E-diene (jatrophane 2), a derivative of a 2,5,7,8,9,14-hexaacetoxy-3-benzoyloxy-15-hydroxy-jatropha-6(17),11E-diene, a 2,5,14-triacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxy-9-nicotinoyloxy-jatropha-6(17),11E-diene (jatrophane 3), a derivative of a 2,5,14-triacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxy-9-nicotinoyloxy-jatropha-6(17),11E-diene, a 2,5,9,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxyjatropha-6(17),11E-diene (jatrophane 4), a derivative of a 2,5,9,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-7-isobutyroyloxyjatropha-6(17),11E-diene, a 2,5,7,14-tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-9-nicotinoyloxyjatropha-6(17),11E-diene (jatrophane 5), a derivative of a 2,5,7,14-

tetraacetoxy-3-benzoyloxy-8,15-dihydroxy-9-nicotinoyloxyjatropha-6(17),11E-diene, a 2,5,7,9,14-pentaacetoxy-3-benzoyloxy-8,15-dihydroxyjatropha-6(17),11E-diene (jatrophane 6), a derivative of a 2,5,7,9,14-pentaacetoxy-3-benzoyloxy-8,15-dihydroxyjatropha-6(17),11E-diene, a 20-O-acetyl-ingenol-3-angelate, a derivative of a 20-O-acetyl-ingenol-3-angelate and pharmaceutically acceptable salt of one or any combination of these compounds.

81. The method of claim 78, wherein the compounds are provided in the form of a chemical fraction obtained from the sap of a species of *Euphorbia*.

82. The method of claim 33, wherein the compound further comprises a beta-alanine betaine or a hydroxy-dimethyl proline.

83. The method of claim 33, wherein the compound is capable of inhibiting or retarding the growth of MM96L cells.

84. The method of claim 33, wherein the compound is capable of inducing differentiation of MM96L cells.

85. The method of claim 33, wherein the compound is capable of inducing normal melanocytes to proliferate.

86. The method of claim 33, wherein the compound is capable of inducing T cells to proliferate.

87. The method of claim 33, wherein the compound is capable of inducing the expression of G-CSF.

88. The method of claim 33, wherein the compound is capable of inducing the expression of major histocompatibility complex (MHC) molecules.

89. The method of claim 33, wherein the compound is capable of recruiting a natural killer cell to a region of application of the compound.

90. The method of claim 33, wherein the compound is capable of a T cell to a region of application of the compound.

91. The method of claim 33, wherein the compound is provided in the form of a composition comprising a pharmaceutically- or cosmetically-acceptable carrier.

92. The method of claim 91, wherein the pharmaceutically- or cosmetically-acceptable carrier is selected from a β-alanine betaine hydrochloride and a t-4-hydroxy-N,N-dimethylproline.

93. A method of recruiting an immune cell to a region of application of a compound, the method comprising administering an effective amount of the compound to the region,

wherein the compound is derived from an extract from the sap of a species of *Euphorbia*, wherein the compound

(a) is extractable from the *Euphorbia* sap in the presence of about 95% v/w ethanol,

(b) has cell inhibiting or retarding activity which is neither destroyed by acetone nor by heating at about 95°C for about 15 minutes, and

(c) is capable of inhibiting the growth of at least one cell line selected from the group consisting of MM96L, MM229, MM220, MM537, MM2058, HeLa, B16, LIM1215, A549, MCF7, MCC16 and Colo16.

94. The method of claim 93, wherein a natural killer cell is recruited to the region of application of the compound.

95. The method of claim 93, wherein a T cell is recruited to the region of application of the compound.--